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EXAMINER	
ZISKA	

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 5/10/96

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), ~~or thirty days~~, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-7, 23-31, is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-7, 23-31 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

This application should be reviewed for errors.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 23-28 have been cancelled. Claims 1-6 and 29-31 are active and examined in this Office Action. It is noted at the outset that the amendment of claim 7 to now claim the gene is improper since administration of genetic material was the basis of one grouping of the restriction requirement, set forth in paper No. 5. The claim is therefore withdrawn from consideration as being directed to a non-elected invention.

The declaration of Dr. Reynolds is acknowledged and has been considered. The declaration does not overcome the rejections directed to administration of growth factors in vivo.

Claim 29 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "progeny culturing said progeny" is vague and unclear; presumably the first "progeny" should be removed.

The rejection of claims 1-6 and 23-31 under 35 U.S.C. 112, first paragraph, is maintained. Applicants have argued that the declaration provides evidence that neural stem cells were obtained from adult human tissue and cultured in vitro; that the present specification teaches that the techniques used to proliferate and differentiate CNS stem cells in vitro can be adapted to achieve similar results in vivo; and cite page 13, lines 20 et seq., for support. However, the cited location discloses in vitro culture and fails to provide evidence that the same in vitro techniques would be sufficient in vivo to obtain the claimed effect.

Applicants have argued that example 1 teaches the extent of in vivo proliferation of mouse neural stem cells in the presence of EGF. However, claim 1 is not limited to EGF.

Applicants have argued that it is expected that since the same procedures result in the proliferation of mouse and human neural stem cells in vitro, a procedure that induces the in vivo proliferation in vivo mouse neural stem cells in vivo could be used to induce proliferation of human neural stem cells. However, the state of the art at the time the claimed invention was made recognized that extrapolation of results between species was unpredictable. See, for example, Emerich, teaching the unpredictability as seen in treatments of neural diseases of other experimental animals such as rats and monkeys.

Applicants have argued they are not required to submit clinical evaluations of treatment in order to establish patentability. Although true, the specification remains nonenabling for practice of the invention in humans for reasons set forth in the previous Office Action.

Applicants have argued that the declaration of Dr. Reynolds establishes that the precursor cells of the subventricular zone of primate lateral ventricle are responsive to growth factors and that similar to mouse studies, growth factor infusion into the adult primate brain results in a dramatic increase in the endogenous subependymal neural precursor cell populations and stimulates their migration away from the lateral ventricle walls into adjacent normal brain parenchyma. However, while humans are primates, not all primates are human and Emerich discloses the unpredictability of extrapolating results obtained from rats and monkeys to humans. The claims are not limited to non-human primates.

Applicants have argued that their invention is designed to overcome the problems discussed by Emerich by inducing the patient's own cells to recover and, for example, to produce dopamine. However, there is no support in the present application, despite reference to copending applications, that

the stem cells could be treated in vivo to proliferate, differentiate and thereby result in dopamine producing cells.

The rejection of claims 1, 2 and 4-6 under 35 U.S.C. 103 as being unpatentable over Smart taken with Williams and Morrison is maintained. The Morshead article is withdrawn as a reference. Applicants have argued that the at the time of the invention, it was the belief in the field that neural stem cells were not found in the adult brain. However, the claims are not limited to the adult brain.

Applicants have argued that it is likely that Smart labelled a population of constitutively proliferating cells and that the cells are distinct from the neural stem cell population. However, turn-over rates per se are not indicative of different cell populations since clearly stimulation of neural stem cells would result in faster proliferation than natural turn-over, lacking evidence to the contrary.

Applicants have argued that neither of Cattaneo or Morrison cure the deficiency of the Smart article. However, Smart discloses that the subependymal layer is a collection of undifferentiated mitotically active cells which persist into adult life. Applicants have argued that neither of Cattaneo or Morrison describe the proliferation of neural stem cells.However, Smart discloses that the subependymal cells are CNS precursor cells. Contrary to applicant's arguments, the references render obvious the invention as currently claimed.

The rejection of claim 3 under 35 U.S.C. 103 as being unpatentable over Smart taken with Williams and Morrison as applied to claims 1, 2, 4-6 and further in view of Cattaneo is maintained; the rejection of claim 7 under 35 U.S.C. 103 as being unpatentable over Smart taken with Williams and Morrison as applied to claims 1, 2, 4-6 and further in view of Williams is maintained; the rejection of claims 29-31 under 35 U.S.C. 103 as being unpatentable over Smart taken with Williams, Cattaneo and

Morrison as applied to claims 1, 2, 4-6 and further in view of Gage is maintained.

No claim is allowed.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO FAX center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (30 November 15, 1989). The CM1 Fax Center number is (703) 308-4227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Suzanne Ziska, Ph.D., whose telephone number is (703)308-1217. In the event the examiner is not available, the examiner's supervisor, Ms. Jacqueline Stone, may be contacted at phone number (703) 308-3153.

SUZANNE E. ZISKA
PRIMARY EXAMINER
GROUP 1800